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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/516,818

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Junzo Tanaka

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07/22/2009

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EXAMINER

NAFF, DAVID M

ART UNIT

PAPER NUMBER

1657

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/516,818

**Applicant(s)**

TANAKA ET AL.

**Examiner**

David M. Naff

**Art Unit**

1657

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 9-11 and 14-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9-11 and 14-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been  
5 timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/23/09 has been entered.

An amendment filed 4/23/09 amended claims 9, 11, 15 and 17.

Claims examined on the merits are 9-11 and 14-17, which are all claims in the application.

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### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

20

Claim 15 is unclear by not claiming a complete method. For example, in addition to alternatively soaking, the method should require the step of alternatively soaking to produce a gradient of calcium phosphate.

### ***Response to Arguments***

While claim 15 has been made independent, the claim omits forming a calcium phosphate gradient, which the specification discloses is required.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-11 and 14-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mattern et al (6,969,523) or Yannas et al (4,947,840) in view of Akashi et al (6,387,414) and Sherwood et al (6,454,811), and if necessary in further view of Taguchi et al (Biomaterials).

The claims are drawn to a composite material containing a gradient of calcium phosphate in a biodegradable polymeric material selected from collagen, glycosaminoglycan and a composite of collagen and glycosaminoglycan having a first and second side, produced by alternatively soaking the second side in a calcium ion-containing solution and in a phosphate ion-containing solution. Also claimed is a method of making the composite by providing the polymeric material and alternatively soaking the second side in a calcium ion-containing solution and in a phosphate ion-containing solution.

Mattern et al (col 1, lines 11-30 and col 3, lines 50-67) and Yannas et al (paragraph bridging cols 1 and 2) disclose scaffolds formed of cross-linked collagen and glycosaminoglycan.

5 Akashi et al disclose preparing a hydroxyapatite composite by alternatively soaking a surface of a matrix in a calcium ion-containing solution and in a phosphate ion-containing solution. Matrices that can be used include collagen and a mucopolysaccharide such as hyaluronic acid (col 4, lines 15-17). The composite has a composition similar to bone and is useful as an artificial tissue such as artificial bone, or as medical materials (col 1, lines 6-12).

10 Sherwood et al disclose (col 4, lines 13-26 and 40-45) forming a gradient of calcium phosphate in a material such as collagen (col 8, line 50) to provide a composite implantable device for regeneration of bone.

Taguchi et al disclose preparing an apatite coating on hydrophilic polymer-grafted poly(ethylene) films by alternate soaking of the film in a calcium ion-containing solution and phosphate ion-containing solution. The resultant composite may be used as a hard tissue substitute and as a soft tissue adhesive.

It would have been obvious to provide hydroxyapatite in the cross-linked collagen/glycosaminoglycan scaffold of Mattern et al or Yannas et al by alternatively soaking the scaffold in a calcium ion-containing solution and a phosphate ion-containing solution as suggested by Akashi et al to provide a composite for use as artificial tissue such as artificial bone, and as suggested by Sherwood et al to make an implantable composite for bone regeneration. Hydroxyapatite is a calcium phosphate compound disclosed in the present specification (page 5, line 22) that can be the calcium phosphate of the claims. Using alternative soaking as disclosed by Akashi et al only on one side of the scaffold of Mattern et al or Yannas et al would have been obvious when hydroxyapatite is desired at only one side, and

subjecting one side to the alternative soaking will inherently provide a gradient of calcium phosphate as claimed. Moreover, Sherwood et al would have suggested a gradient.

Components of claim 11 would have been obvious since the components and their functions are known, and it would have been obvious to provide the components in a scaffold to obtain their expected functions. Providing cells as required by claim 14 would have been obvious to obtain the function of the cells to generate tissue. The scaffold of Mattern et al or Yannas et al is inherently porous as required by claim 16. If needed, Taguchi et al would have further suggested using alternate soaking as claimed to provide calcium phosphate in the scaffold of Mattern et al or Yannas et al.

***Claim Rejections - 35 USC § 103***

Claims 9, 15, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akashi et al.

The invention and Akashi et al are described above.

When preparing the hydroxyapatite composite of Akashi et al by alternatively soaking a surface of a matrix in a calcium ion-containing solution and in a phosphate ion-containing solution, it would have been obvious to use collagen as the matrix as suggested by Akashi et al disclosing that the matrix can be collagen. A gradient as required by the present claims will inherently result.

***Claim Rejections - 35 USC § 103***

Claims 10, 11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akashi et al in view of Mattern et al or Yannas et al.

Claim 10 requires the polymeric material to be a crosslinked product of glycosaminoglycan and collagen.

Mattern et al and Yannas et al are described above.

It would have been obvious to replace the collagen of Akashi et al with the cross-linked collagen/glycosaminoglycan suggested by Mattern et al or Yannas et al to obtain the function of glycosaminoglycan in addition to collagen. Components of claims 11 and 13 would have been obvious since the components and their functions are known, and it would have been obvious to  
5 provide the components in a scaffold to obtain their expected functions. Providing cells as required by claim 14 would have been obvious to obtain the function of the cells to generate tissue.

### ***Response to Arguments***

The amendment urges that Akashi et al do not produce a gradient since the entire matrix  
10 is alternatively soaked. However, soaking the entire matrix will not prevent forming a gradient since the gradient can extend from the entire surface of the matrix towards the center of the matrix. In any event, using alternative soaking as disclosed by Akashi et al only on one side of the scaffold of Mattern et al or Yannas et al would have been obvious when hydroxyapatite is desired at only one side, and subjecting one side to the alternative soaking will inherently  
15 provide a gradient of calcium phosphate as claimed. Moreover, Sherwood et al would have suggested a gradient.

When the material is collagen disclosed by Akashi et al (col 4 line 15) or cross-linked collagen and glycosaminoglycan disclosed by Mattern et al or Yannas et al, the material is porous, and soaking will inherently result in calcium and phosphate ions being absorbed into the  
20 material and forming a gradient where the concentration of calcium phosphate is higher at the surface contacted with the calcium and phosphate ions and decreases towards to the other side. Taguchi et al (Biomaterials) disclose (page 3, 2nd complete paragraph) forming bone-like apatite on/in in a three-dimensional hydrogel matrix by alternative soaking. This supports that calcium phosphate will be formed both at the surface and inside a porous matrix when subjected

to the alternative soaking. When alternatively soaking one side, which is obvious as set forth above, the surface of this side can be considered a second side, and a greater amount of calcium phosphate will obviously be at this side since this side has the surface that is contacted with the alternative soaking solutions. When soaking the whole material as disclosed by Akashi et al and Taguchi et al, the surface of the whole material contacted with the alternative soaking solutions has the greater amount of calcium phosphate as when the second side is contacted with the alternative solutions. An unexpected result is not seen from contacting one side of a material alternatively with calcium and phosphate solutions as claimed as compared to contacting a whole material alternatively with calcium and phosphate solutions as disclosed by Akashi et al and Taguchi et al. Alternative soaking of a whole material will result in a gradient from the surface to within the interior of the material when the material is porous. Both methods result in a hydroxyapatite composite that can be used as an implant, and soaking only one side has not been established to provide a composite having a different function.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David M. Naff/  
Primary Examiner, Art Unit 1657

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DMN  
7/20/09